One pill can kill

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Objectives

-Become familiar with toxins that can harm children in small doses

-Discuss the mechanism of toxicity of these agents

-Develop a treatment strategy for these toxins

• Most exposures nontoxic
• Unintentional
• Few meds cause toxicity in small doses

Low dose killers

• Calcium channel blockers
• Clonidine
• Cyclic antidepressants
• Opioids
• Sulfonylureas
• Camphor
• Salicylates
• Toxic alcohols
• Antimalarials

• Calcium Channel Blockers

• Types of CCB
  • Dihydropyridines (Nifedipine)
  • Phenylalkylamine (verapamil)
  • Benzothiaprines (diltiazem)

• Antagonize L-type voltage sensitive
  • Cardiac and smooth muscle

• Selectivity lost in overdose

• Mechanism of CCB
• Clinical Toxicities: CCB
• Hypotension (most common)
• Bradycardia
• Hyperglycemia
  • Peripheral insulin resistance
  • Ca-dependent Pancreatic insulin release
• Rapid clinical deterioration
  • Regular release: 2-3 hours
  • SR: > 6 hours
• Treatment
• Decontamination
  • ? Activated charcoal
  • WBI
• IV Fluid resuscitation
• Atropine
• Calcium increased to 12-15 mg/dL
• Treatment
• High Insulin Euglycemia
  • 1u/kg/hr gtt
  • Substrate for stressed heart
  • Inotrope and vasodilator
  • Helps with insulin resistance
• Lipid Emulsion Therapy
  • Low dose killers
• Calcium channel blockers
• Clonidine
• Cyclic antidepressants
• Opioids
• Sulfonylureas
- Camphor
- Salicylates
- Toxic alcohols
- Antimalarials
- Clonidine (an imidazoline)
- A2-adrenergic agonists
  - Impairs release of NE
  - sympatholytic
- Imidazoline receptors
- Available in pills and patches
- Toxicity
- Symptoms within 30-90 minutes
- Opioid-like toxidrome
  - Respiratory depression/ intermittent apnea
  - Miosis
  - Bradycardia
  - Hypotension
  - *Altered mental status*
- Treatment
- Decontamination
- ECG/cardiac monitoring
- Treat hypotension and bradycardia
- Apnea observation
- ? Naloxone
- Low dose killers
- Calcium channel blockers
- Clonidine
- Cyclic antidepressants
- Opioids
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- Antimalarials
- Tricyclic antidepressants

- **Uses**
  - Chronic pain
  - ADHD
  - Neuropathic pain

- **< 6 y.o**
  - 10% exposures

- **Tricyclics MOA**
  - Inhibit reuptake of neurotransmitters
  - Na+ channel blockade
  - Alpha -1 antagonism
  - Antimuscarinic
  - Anti-GABA
  - Block K+ rectifier channel blockade

- **Toxicity**
  - Quick onset and rapid deterioration

- **CNS**
  - Altered mental status
  - Seizures

- **Cardiovascular**
  - Hypotension
  - Prolonged QT/dysrhythmias
  - Tachycardia
• QRS > 100ms as marker for toxicity

• Treatment

• Indications
  • QRS > 100ms, tachycardia, hypotension

• NaHCO₃-
  • 1-2meq/kg boluses
  • Overcome Na+ channel blockade
  • Low pH increases free drug → tissue toxicity
  • Goal pH 7.4-7.5

• Treatment

• Hypotension
  • Norepinephrine

• Altered mental status
  • Anticipate seizures
  • Early intubation

• Dysrhythmias
  • Lidocaine

• End-point
  • Resolution of cardiovascular toxicity

• Low dose killers

• Calcium channel blockers

• Clonidine

• Cyclic antidepressants

• Opioids

• Sulfonylureas

• Camphor

• Salicylates

• Toxic alcohols

• Antimalarials
• Opioids
• Can be ingested in combo with APAP
• MOA:
  • Agonists of opioid receptors \( \mu, \delta, \kappa \)
  • \( \mu \) receptor – respiratory depression
• \( \sim 1 \text{mg/kg} \) can lead to toxicity
  • Toxicity
• Onset of symptoms within one hour
• Opioid toxidrome
  • CNS depression
  • Respiratory depression
  • Miosis
  • Treatment
• Observe for minimum six hours
• WBI
• Naloxone for respiratory suppression
  • Competitive antagonist
  • Reverses respiratory and CNS sx
  • Lasts 20-90 minutes
  • May need repeat dosing
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• Oral hypoglycemics
• Long duration of action
• Delayed onset hypoglycemia
  • Chlorpropamide
  • Glipizide
  • Glyburide
• Mechanism of action
• Bind K+ channel
• Prevent K+ efflux
• Increased cell potential
• Ca+ influx
• Insulin release
• Toxicity and Treatment
• Symptoms of hypoglycemia
  • CNS
• Sequelae: permanent neuro impairment/death
• Asymptomatic treatment
• Eat
• No IV dextrose
• Q1 hour blood sugar checks x 12 hours

• Treatment: symptomatic dextrose, octreotide

  Low dose killers

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• Camphor
  (aromatic terpene ketone)

• Found in many OTC products
  • Vaporized cold medications
  • Cold sore preparations
  • Topical Musculoskeletal preparations

• 75% of exposures in children <6 y.o

• Toxicity from misuse
  • Eating product
  • Toxicity
  • MOA unknown

• Rapid onset (5-30 minutes)

• Exposure
  • Dermal
  • Inhalation
• **Ingestion**
  
  • 1 gram can cause serious toxicity
  
  • Oropharyngeal burns
  
  • **Seizures**
  
  • Treatment
  
  • No charcoal
  
  • Remove source of exposure
  
  • Observe for 4 hours
    
    • If no sx, unlikely to develop
  
  • Treat seizures with benzos and barbiturates
  
  • Mortality from seizures and respiratory suppression
  
  • Low dose killers
  
  • Calcium channel blockers
  
  • Clonidine
  
  • Cyclic antidepressants
  
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  • Salicylates
  
  • Toxic alcohols
  
  • Antimalarials
  
  • Salicylates
  
  • Found in:
    
    • ASA
    
    • Oil of wintergreen
    
    • Pepto-bismol (small)
  
  • **MOA:**
    
    • Uncoupling of oxidative phosphorylation
    
    • Anerobic respiration → lactic acid accumulation
- Weak acids accumulate

- **Toxicity**
  - Toxic ingested dose 150mg/kg
    - 1 ml oil of Wintergreen
    - ASA tablets
  - Signs and sx at 30mg/dL

- **Laboratory findings**
  - Anion gap metabolic acidosis
  - Ketonuria
  - Elevated aspirin level
  - Hypokalemia

- **Treatment**
  - **Decontamination**
    - MDAC 0.5g/kg q 2-4 hours x 12 hours
  - Serum alkalization, pH >7.4
    - ASA weak acid
    - Ion trap ASA $[HA] \rightarrow [H^+] + [A^-]$
    - Prevents formed ASA into tissues
    - Enhance urinary excretion

- **Treatment**
  - Hemodialysis
    - Pulmonary edema
    - Altered mental status
    - ASA level > 100 mg/dL
    - Persistent acidosis
    - Low dose killers

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**Symptoms**
- CNS depression
- Gastritis

**Laboratory findings**
- Osmolar gap
  - \(2(Na^+) + \text{BUN}/2.8 + \text{glucose}/18\)
- Anion gap metabolic acidosis
  - Not in isopropyl

**Treatment**
- Inhibit enzyme alcohol dehydrogenase
  - Ethanol - outcompetes
  - Fomepizole
  - Excrete parent compound
  - Hemodialysis
  - Significant metabolic acidosis
  - Renal insufficiency
  - Low dose killers

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• Antimalarials
• <1000 cases/year
• Chloroquine
  • >5g -> potentially fatal
  • Death in 12 hours
  • Cardiac toxicity – hypotension, Na+ and K+ channels
  • Hypokalemia – direct intracellular shifts
  • Neurotoxicity – CNS depression
• Antimalarials
• Quinine
  • Cardiac toxicity – inhibits K+ and Na+ channels
  • Ototoxicity – toxic to Organ of Corti
  • Ocular toxicity - direct retinal toxicity
  • Pancreatic - hypoglycemia
• Treatment
• Quinine
  • Sodium Bicarbonate
  • Monitor for TdP
• Chloroquine
  • Epinephrine
  • Valium
  • Sodium Bicarbonate
• Summary